REMARKS

Claims 8-10 and 15 have been amended and claims 23-25 have been added. Claims 8-12, 15, 16, and 23-25 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 1, line 22; page 4, lines 20-24; page 5, lines 18-20; page 9, lines 8-10; page 10, lines 5-8; page 14, line 37 to page 15, line 3; and in Tables 1, 3, and 5. No new matter has been added as a result of the above-described amendments. The objections and rejections set forth in the Office Action have been overcome by amendment.

1. Rejections of claims 8-16 under 35 U.S.C. § 112, second paragraph

The Office Action maintains a rejection of claims 8-16 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. In particular, the Action maintains that the recitation of the terms "high-risk HPV DNA" and "low-risk HPV DNA" renders the metes and bounds of the pending claims unclear.

The Office Action mailed May 24, 2006 asserted that originally-filed claims 8-16 were indefinite since originally-filed claim 8 recited "high-risk HPV DNA" and "low-risk HPV DNA," and neither the claims nor the art set forth a standard for determining whether an HPV type is a high-risk type or a low-risk type. The instant Action acknowledges that while the terms "high-risk HPV DNA" and "low-risk HPV DNA" may be commonly used in the prior art, the use of such terms does not clearly describe the metes and bounds of the pending claims. The instant Action notes, for example, that the Light *et al.*, 1998 reference refers to HPV type 70 as an "oncogenic HPV type," but that the American Society for Colposcopy and Cervical Pathology describes this type as a low-risk HPV type that is virtually never found in cancers.

Applicants first note that while the originally-filed claims recited the term "high-risk HPV DNA," the claims pending in the instant application were amended in Applicants' response to the Action mailed May 24, 2006 to delete reference to the term "high-risk HPV DNA." As for the recitation of "low-risk HPV DNA," Applicants have amended claim 8 to recite that "the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of HPV types 42, 43, or 44." Support for this amendment can be found in the specification at, for example, page 1, line 22;

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page 4, lines 20-24; page 5, lines 18-20; page 10, lines 5-8; page 14, line 37 to page 15, line 3; and in Tables 3 and 5. In particular, the specification demonstrates that a reagent comprising genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, and 51 cross-hybridizes with the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70, and does not cross-hybridize with the genomic sequences of HPV types 42, 43, or 44. Applicants contend that the rejection based on 35 U.S.C. § 112, second paragraph, has been overcome by amendment, and therefore, respectfully request that this rejection be withdrawn.

Before addressing the Action's written description and enablement rejections, and in order to expedite the pending claims to allowance, Applicants wish to point out that the data presented in Table 1 of the specification in no way contradicts the specification's other teachings. In particular, the data presented in Table 1 was generated by analyzing cell samples containing a known HPV strain with **individual** genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, or 51, and not a reagent comprising all six of these genomic HPV DNA probes. Thus, the fact that a non-reduced amount of a genomic HPV type 16 DNA probe, when used in isolation, exhibits some cross-reactivity with HPV types 42, 43, and 44, or the fact that a non-reduced amount of a genomic HPV type 31 DNA probe, when used in isolation, exhibits some cross-reactivity with HPV type 42, is not relevant to the method of claim 8. In fact, Applicants note that it was the experimental results described in Example 1 of the specification that which led them to reduce the proportions of genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 in the six probe cocktail, thereby eliminating undesired cross-reactivity with certain HPV types (*see* Supplemental Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo submitted with respect to U.S. Application No. 09/582,492, para. 4).

2. Rejections of claims 8-12, 15, and 16 under 35 U.S.C. § 112, first paragraph

a. Rejection of claims 8-12, 15, and 16 under the written description requirement of 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 9 and 10 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application

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was filed, had possession of the claimed invention.

i. "proportion of total HPV DNA in the reagent..."

The Action asserts that the limitation in claim 9 that recites "the proportion of total HPV DNA in the reagent that comprises nucleic acid fragments of the first genomic HPV DNA probe set and the proportion of total HPV DNA in the reagent that comprises nucleic acid fragments of the third genomic HPV DNA probe set are decreased relative to the proportions of the total HPV DNA in the reagent" represents new matter. The Action states that the specification discloses but one example of a reagent suitable for practicing the method of claim 9, and neither discusses nor contemplates other reagents encompassed by claim 9. The Action also states that while claim 9 sets forth general requirements that HPV types 16 and 31 have lower representation in the probe reagent, this disclosure is still quite broad because it allows for any possible proportions within this generic requirement. The Action therefore concludes that claim 9 incorporates new matter.

Applicants respectfully disagree with the Action's assertion that no there is no specific basis for the above limitation in the specification, and that, as a result, claim 9 incorporates new matter. Applicants note first that the phrase "nucleic acid fragments of the first genomic HPV DNA probe set" refers to a genomic HPV type 16 DNA probe set, and the phrase "nucleic acid fragments of the third genomic HPV DNA probe set" refers to a genomic HPV type 31 DNA probe. Applicants also note that one of ordinary skill in the art would recognize that the phrase "nucleic acid fragments of the other HPV DNA probe sets" refers to genomic HPV DNA probe sets prepared from the genomic sequences of HPV types 18, 33, 35, and 51. Thus, the skilled artisan would understand that the above limitation describes a probe reagent in which the genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 are reduced relative to the genomic HPV DNA probes prepared from the genomic sequences of HPV types 18, 33, 35, and 51.

Applicants contend that support for this limitation can be found in the specification's disclosure that undesired cross-reactivity observed with genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 can be essentially nullified by reducing the concentration (or proportions) of these two genomic HPV DNA probes in the probe reagent (*see, e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). While the specification discloses

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one example of a reagent comprising genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, and 51, which cross-hybridizes with the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70 and does not cross-hybridize with the genomic sequences of HPV types 42, 43, or 44, the specification also clearly provides the **first** teaching in the art that the concentrations of the genomic sequences of HPV types 16 and 31 must be lowered in order to eliminate undesired cross-reactivity (*see* Supplemental Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo, para. 5). With respect to the method of claim 9, which depends from claim 8, the undesired cross-reactivity to be eliminated is represented by the limitation of claim 8 that the labeled nucleic acid fragments of the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of HPV types 42, 43, or 44.

In view of the teachings of the specification, the skilled artisan would recognize that the concentrations of the genomic sequences of HPV types 16 and 31 must be lowered in order to eliminate undesired cross-reactivity, and that the undesired cross-reactivity could be eliminated using reagents other than that depicted in Table 2. In other words, the skilled artisan would recognize that the inventors had possession of more than just the single reagent depicted in Table 2, and instead, had possession of all reagents in which the genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 are reduced relative to the genomic HPV DNA probes prepared from the genomic sequences of HPV types 18, 33, 35, and 51, such that the genomic HPV DNA probe sets detectably hybridize to the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70 but not to the genomic sequence of HPV types 42, 43, or 44 (*see* Supplemental Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo, para. 6).

Applicants, therefore, contend that the limitation set forth above is fully supported by the specification and does not represent new matter. Withdrawal of this ground of rejection is therefore respectfully solicited.

ii. "about"

The Action also asserts that the recitation in claim 15 of "about 8.3%" and "about 20.8%" appear to be new matter because the specification does not provide any basis for modification of the percentages.

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As described in section 2(i) above, support for the terms "about 8.3%" and "about 20.8%" can be found in the specification's disclosure that undesired cross-reactivity observed with genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 can be essentially nullified by reducing the concentration (or proportions) of these two genomic HPV DNA probes in the probe reagent (*see, e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). While the specification discloses one example of a reagent comprising genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, and 51, which cross-hybridizes with the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70 and does not cross-hybridize with the genomic sequences of HPV types 42, 43, or 44, the specification also clearly provides the **first** teaching in the art that the concentrations of the genomic sequences of HPV types 16 and 31 must be lowered in order to eliminate undesired cross-reactivity (*see* Supplemental Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo, para. 5). With respect to the method of claim 15, which depends from claim 8, the undesired cross-reactivity to be eliminated is represented by the limitation of claim 8 that the labeled nucleic acid fragments of the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of HPV types 42, 43, or 44.

In view of the teachings of the specification, the skilled artisan would recognize that the concentrations of the genomic sequences of HPV types 16 and 31 must be lowered in order to eliminate undesired cross-reactivity, and that the undesired cross-reactivity could be eliminated using reagents other than that depicted in Table 2. In other words, the skilled artisan would recognize that the inventors had possession of more than just the single reagent depicted in Table 2, and instead, had possession of all reagents in which the genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 are reduced relative to the genomic HPV DNA probes prepared from the genomic sequences of HPV types 18, 33, 35, and 51, such that the genomic HPV DNA probe sets detectably hybridize to the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70 but not to the genomic sequence of HPV types 42, 43, or 44 (*see* Supplemental Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo, para. 6). Thus, confining applicants to the specific probe concentrations indicated in Table 2 ignores the teachings of the specification (*i.e.*, that undesired cross-reactivity can be eliminated by reducing the concentrations of the genomic sequences of HPV types 16 and 31 in the reagent), deprives applicants of the claim scope to which

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they are entitled, and provides a simple blueprint for Applicants' competitors to avoid infringement.

Applicants, therefore, contend that the terms "about 8.3%" and "about 20.8%" in claim 15 are fully supported by the specification and does not represent new matter. Withdrawal of this ground of rejection is therefore respectfully solicited.

iii. "is hybridized"

The Action also asserts that the recitation in claim 10 that the reagent "is hybridized" represents new matter. The Action states that while the specification discloses conditions for a post-hybridization wash, the specification does not disclose hybridizing the reagent at the conditions recited in claim 10.

Applicants have amended claim 10 to recite "wherein hybridization conditions comprise washing the cell sample at 45°C in a buffer comprising 2X SSC and 2% BSA." Applicants note that the specification explicitly discloses the use of these post-hybridization wash conditions (*see, e.g.*, page 14, lines 29-30). Applicants contend that amended claim 10 is fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

iv. "detectably hybridize to . . . a low-risk HPV type"

The Action also asserts that the functional limitation in claim 8 that "the nucleic acid fragments of the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of a low-risk HPV type" fails to satisfy the written description requirement because the specification does not describe a reagent that does not detectably hybridize to the genomic sequence of a low-risk HPV type. In particular, the Action states that even the most preferred reagent described in the specification hybridizes, in some cases, to low-risk HPV types. The Action notes, for example, that the specification discloses that individual genomic HPV DNA probes prepared from HPV types 16, 18, 31, 33, 35, and 51 cross-hybridize to some degree with other HPV types, including in some cases, low-risk HPV types. The Action also notes that the "present probe cocktail" described in Example 1 of the specification was shown to detectably hybridize to a single patient sample containing HPV type 6/11 DNA (as well as to three patient samples containing HPV type 70 DNA). The Action further notes that the probe solution described in Example 3 of the specification was

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shown to detectably hybridize to patient samples containing HPV type 70 DNA under either high stringency or low stringency post-hybridization wash conditions.

As described above in section 1, Applicants have amended claim 8 to recite that "the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of HPV types 42, 43, or 44." Applicants note that the specification discloses that a reagent comprising genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, and 51 cross-hybridizes with the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70, and does not cross-hybridize with the genomic sequences of HPV types 42, 43, or 44 (*see, e.g.*, page 4, lines 20-24; page 5, lines 3-4 and 18-20; page 8, lines 27-29; page 10, lines 5-8; page 14, line 37 to page 15, line 3; and in Tables 3 and 5). Applicants contend that amended claim 8 is fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

v. "essentially the full-length genomic sequence "

The Action also asserts that the limitation in claim 8 that a plurality of nucleic acid fragments of a genomic HPV DNA probe set "detectably hybridize to a plurality of different nucleotide sequences of essentially the full-length genomic sequence" of a particular HPV type fails to satisfy the written description requirement because the limitation is extremely broad as to how much of the essentially full-length genomic sequence of a particular HPV type must be hybridized to the plurality of nucleic acid fragments of the genomic HPV DNA probe set.

Applicants respectfully disagree with the Action's assertion that the limitation set forth in the preceding paragraph is not supported by an adequate written description. Nevertheless, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect in the proper scope of the pending claims, Applicants have amended claim 8 to recite that the HPV DNA probe sets comprise "a plurality of labeled nucleic acid fragments prepared by labeling essentially the full-length genomic sequence" of a particular HPV type. Applicants contend that the above language is fully supported by the specification.

In particular, Applicants note that the specification discloses a reagent comprising a cocktail of genomic HPV DNA probes, and methods for using this reagent. Applicants contend that a skilled artisan would readily understand the meaning of the term "genomic HPV DNA probe." Evidence

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that the term "genomic HPV DNA probe" has an established meaning in the art can be found, for example, in references cited in the Office Action mailed May 24, 2006 (*see, e.g.*, Nuovo, 1998, *Diagnostic Molecular Pathology* 7:158-63 and Nuovo *et al.*, 1995, *J. Histotechnology* 18:105-10).

Applicants contend that the specification's teachings that the genomic HPV DNA probes of the invention are "essentially full-length genomic HPV probes," that "some . . . shortening of the probe length are permitted," and that the genomic HPV DNA probes of the invention "range from roughly 6000 to 8000 base pairs" (*see, e.g.*, page 4, line 21; page 5, lines 3, 9-10, and 13-14) must be read in the light of the understanding in the art regarding the meaning of the term "genomic HPV DNA probe" and the specification's teachings regarding the preparation of such probes (*see, e.g.*, page 8, lines 27-34). Applicants, therefore, contend that one of ordinary skill in the art would understand that the genomic HPV DNA probes of the invention could readily be prepared from plasmids containing something less than the entire full-length genomic sequence of a particular HPV type (for example, 6000 of the approximately 8000 nucleotides in that genomic sequence). Applicants contend that amended claim 8 is fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

vi. Proportions of claim 15

The Action also asserts that the recitation in claim 15 of the proportions of each genomic HPV DNA probe in the reagent does not remedy the problems discussed above in section 2(a)(i). In particular, the Action states that claim 15 fails to satisfy the written description requirement because the specification lacks an adequate written description "as to how much actual HPV genomic sequence must be represented in each individual probe set." The Action also states that the specification does not disclose reagents having proportions other than those recited in claim 15.

Applicants respectfully disagree with the Action's assertion that the recitation of proportions in claim 15 fails to satisfy the written description requirement. Applicants note that the specification discloses these exact proportions (*see* Table 2) and probe concentrations corresponding to these proportions (*see* page 13, lines 24-27). Moreover, as discussed above in section 2(a)(i), the specification discloses that undesired cross-reactivity observed with genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 can be essentially nullified by

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reducing the concentration (or proportions) of these two genomic HPV DNA probes in the probe reagent (*see, e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). Thus, one of ordinary skill in the art would recognize that the reagent composition disclosed in Table 2 could be used to practice the method of claim 8. Moreover, in view of the teachings in the specification, the skilled artisan would understand that the methods of the invention could be practiced using other reagent combinations in which the proportions of the genomic HPV type 16 and 31 probes are either reduced or increased relative to the proportions recited in claim 15. Applicants contend that amended claim 15 is fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

vii. Genomic HPV DNA probes defined by function

The Action also asserts that the claims do not set forth any particular sequences or structure for the recited genomic HPV DNA probes, and only define the recited genomic HPV DNA probes in terms of their function. The Action states that the limitation in claim 8 that the plurality of nucleic acid fragments of the genomic HPV DNA probe sets hybridize to essentially the full-length genomic sequence of a particular HPV type does not limit the length or composition of the probe fragments. As a result, the Action contends that the claims encompass any set of oligonucleotide probes that would specifically hybridize to the recited HPV types. The Action suggests that a 30-mer oligonucleotide probe would be encompassed by the claims since it could hybridize to the full-length genomic sequence of one of the recited HPV types.

Applicants respectfully disagree that the pending claims encompass any set of oligonucleotide probes (such as a 30-mer) that would specifically hybridize to the recited HPV types. As discussed above in section 2(a)(v), Applicants contend that a skilled artisan would readily understand that the methods of the invention utilize genomic HPV DNA probes. Evidence that the term "genomic HPV DNA probe" has an established meaning in the art can be found, for example, in references cited in the Office Action mailed May 24, 2006 (*see, e.g.*, Nuovo, 1998, *Diagnostic Molecular Pathology* 7:158-63 and Nuovo *et al.*, 1995, *J. Histotechnology* 18:105-10). Thus, the claimed methods utilize a reagent containing genomic HPV DNA probes, which are quite different from oligonucleotide probes.

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Nevertheless, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, as well as expedite prosecution of the pending claims to allowance, Applicants have amended claim 8 to recite that the HPV DNA probe sets comprise "a plurality of labeled nucleic acid fragments prepared by labeling essentially the full-length genomic sequence" of a particular HPV type. Support for this amendment is presented above in section 2(a)(v). Applicants contend that in view of the specification's teachings and knowledge in the art at the time the application was filed, one of ordinary skill in the art would readily understand how to prepare the genomic HPV DNA probes of the claimed methods, and further, would be able to prepare a reagent from these genomic HV DNA probe sets that satisfies the limitations of claim 8 (as well as the limitations of the other pending claims). Applicants contend that the pending claims are fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

viii. Critical features of cross-reactivity

The Action also asserts that the specification does not provide any description of the critical features of even the single reagent disclosed in Examples 1 and 3 that would allow that reagent to detectably hybridize to the genomic sequence of HPV types 16, 18, 31, 33, 35, and 51, and additionally, to detectably hybridize to the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70. The Action states that while the specification discloses only one species of the reagent recited in the pending claims, the claims encompass a genus of reagents comprising hundreds of thousands of possibilities. The Action also states that the specification contains no description demonstrating conception of reagents modified from the single example disclosed in the specification but possessing the functional characteristics required by the claims.

Applicants respectfully disagree with the Action's assertion that the specification does not provide any description of the critical features of a reagent that would detectably hybridize to the genomic sequence of HPV types 16, 18, 31, 33, 35, and 51, and additionally, to the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70. As discussed above in section 2(a)(i), the specification discloses that undesired cross-reactivity observed with genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 can be essentially nullified by

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reducing the concentration (or proportions) of these two genomic HPV DNA probes in the probe reagent (*see, e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). As discussed above in section 2(a)(vi), the specification also discloses exemplary proportions for the six genomic HPV DNA probes (*see* Table 2), and probe concentrations corresponding to these proportions (*see* page 13, lines 24-27), that can be used to practice the claimed methods. In view of the teachings in the specification, the skilled artisan would understand that the methods of the invention could be practiced using other reagent combinations in which the proportions of the genomic HPV type 16 and 31 probes are either reduced or increased relative to the exemplary proportions disclosed in the specification. Applicants contend that the pending claims are fully supported by the specification, and therefore, respectfully request that this ground of rejection be withdrawn.

b. Rejection of claims 8-12, 15, and 16 under the enablement requirement of 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 8-12, 15, and 16 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. The Action notes that Applicants' response to the Office Action mailed May 24, 2006 and Declaration Pursuant to 37 C.F.R. § 1.132 of Gerard J. Nuovo argue that one of ordinary skill in the art would not be able to determine the particular HPV types or proportions constituting the reagent disclosed in the Nuovo, 1998 reference without undue experimentation. The Action states that following the reasoning provided in Applicants' response and the Nuovo Declaration, it would require undue experimentation for one of ordinary skill in the art to modify the specific reagent disclosed in the specification to arrive at a reagent that meets the functional limitations of the claims.

In particular, the Action contends that the single reagent disclosed in the specification does not meet the limitations of the claims. The Action also contends that it would require extensive experimentation and screening of samples using reagents with differing compositions to identify reagents that did meet the limitations of the claims. The Action suggests that one of ordinary skill in the art would be forced to vary the "content of the probe sequences," the proportions of the HPV

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genomic probe sets, and even the HPV types included within the reagent. The Action concludes that the instant specification does not provide any further guidance as to how the single disclosed embodiment could be modified to arrive at a reagent that would function in the same way.

Applicants respectfully disagree that the claimed methods are not enabled or that it would require undue experimentation to practice the claimed methods. As Applicants discussed in their response to the Office Action mailed May 26, 2006, and as Dr. Nuovo discussed in his Declaration, the Nuovo, 1998 reference does not disclose the particular HPV types or proportions constituting its reagent. The instant case presents the exact opposite situation.

As discussed above in section 2(a), the specification discloses at least the following: (1) a reagent comprising genomic HPV DNA probes prepared from the genomic sequences of HPV types 16, 18, 31, 33, 35, and 51 that cross-hybridizes with the genomic sequence of HPV types 39, 45, 52, 56, 58, 59, 68 and 70, and which does not cross-hybridize with the genomic sequences of HPV types 42, 43, or 44 (*see, e.g.*, page 4, lines 20-24; page 5, lines 3-4 and 18-20; page 8, lines 27-29; page 10, lines 5-8; page 14, line 37 to page 15, line 3; and in Tables 3 and 5); (2) exemplary proportions for the six genomic HPV DNA probes (*see* Table 2), and probe concentrations corresponding to these proportions (*see* page 13, lines 24-27), that can be used to practice the claimed methods; and (3) that undesired cross-reactivity observed with genomic HPV DNA probes prepared from the genomic sequences of HPV types 16 and 31 can be essentially nullified by reducing the concentration (or proportions) of these two genomic HPV DNA probes in the probe reagent (*see, e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). The Nuovo, 1998 reference provides none of these teachings. Thus, where the Nuovo, 1998 reference does not disclose the particular genomic HPV probes or proportions of HPV types its reagent, the instant application discloses **both** the particular HPV types and the proportions for an exemplary reagent. In view of the specification's teachings that undesired cross-reactivity can be nullified by reducing the concentration (or proportions) of the genomic HPV DNA probes for HPV types 16 and 31, one of ordinary skill in the art could readily make and use the reagents recited in the pending claims without undue experimentation.

Applicants also respectfully disagree with the Action's suggestion that one of ordinary skill in the art would be forced to vary the "content of the probe sequences," the proportions of the HPV genomic probe sets, and even the HPV types included within the reagent. First, the particular HPV

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types comprising the reagent of the claimed methods are explicitly recited in the pending claims. One of ordinary skill in the art would not have to vary the HPV types included in the reagent to make and use the claimed invention, and in fact, a reagent comprising genomic HPV DNA probes prepared from less than the six specific HPV types recited in the claims would not be encompassed by the pending claims. Second, one of ordinary skill in the art would not be "forced" to vary the "content of the probe sequences" or the proportions of the HPV genomic probe sets. While one of ordinary skill in the art could certainly prepare genomic HPV DNA probes using plasmids containing less than the entire full-length genomic sequence of a particular HPV type (for example, 6000 of the approximately 8000 nucleotides of the genomic sequence), such experimentation would not be required to practice the claimed invention. With respect to this last point, Applicants contend that in view of the teachings in the specification, it would be unfair to require them to incorporate the specific percentages recited in claim 15 into claim 8. Clearly, one of ordinary skill in the art would understand that a reagent that satisfies the limitations of the pending claims could be prepared by reducing or increasing the proportions of the genomic HPV DNA probes for HPV types 16 and 31 recited in claim 15.

Applicants also respectfully disagree with the Action's assertion that the instant specification does not provide any guidance as to how the single disclosed embodiment could be modified to arrive at a reagent that would function in the same manner as the single disclosed embodiment. Quite to the contrary, the specification illustrates that equivalent amounts of genomic HPV DNA probes for HPV types 16 and 31, in contrast with those for HPV types 18, 33, 35, or 51, exhibit undesired cross-reactivity (*see*, *e.g.*, Table 1). The specification also explicitly teaches that undesired cross-reactivity can be nullified by reducing the concentration (or proportions) of the genomic HPV DNA probes for HPV types 16 and 31 in the reagent (*see*, *e.g.*, page 9, lines 8-10; page 10, lines 5-8; and Tables 1 and 3). Thus, in view of the teachings in the specification, the skilled artisan would understand that equivalent amounts of genomic HPV DNA probes for HPV types 16 and 31 would result in undesired cross-reactivity, and that such cross-reactivity could be eliminated by reducing the proportions of the genomic HPV DNA probes for HPV types 16 and 31 relative to the genomic HPV DNA probes prepared from the genomic sequences of HPV types 18, 33, 35, and 51. The skilled artisan would also understand from the teachings of the specification and

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knowledge in the art that the proportions set forth in Table 2 are merely exemplary, and that reagents having modified proportions – but in which the genomic sequences of HPV types 16 and 31 are reduced relative to the genomic HPV DNA probes prepared from the genomic sequences of HPV types 18, 33, 35, and 51 – would still exhibit desired cross-reactivity, but not undesired cross-reactivity.

Applicants contends that the rejection based on the enablement requirement of 35 U.S.C. § 112, first paragraph, has been overcome by amendment or traversed by argument, and therefore, respectfully request that this rejection be withdrawn.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Switzer believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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Dated: November 12, 2007

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